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(FILE 'HOME' ENTERED AT 11:34:37 ON 07 APR 2003)

FILE 'KOSMET, IPA, BIOSIS, USPATFULL, CAPLUS' ENTERED AT 11:35:41 ON 07
APR 2003

L1 568 S MUCOADHE##### (5W) POLYMER###
L2 791001 S THIO? OR SULFHYDRYL? OR THIOLATED OR (SULF HYDRYL?)
L3 790999 S THIO? OR SULFHYDRYL? OR THIOLATED OR (SULFA HYDRYL?) OR
SULFA
L4 58 S L3 AND L1
L5 51 DUPLICATE REMOVE L4 (7 DUPLICATES REMOVED)

=> log hold

L5 ANSWER 50 OF 51 USPATFULL
ACCESSION NUMBER: 95:99134 USPATFULL
TITLE: Small peptidic compounds useful for the treatment of glaucoma
INVENTOR(S) : Stig, Aasmul-Olsen, Skodsborg, Denmark
Widmer, Fred, Ryde, Australia
Gauri, Kailash K., Lentfohrden, Germany, Federal Republic of
PATENT ASSIGNEE(S) : Carlbiotech, Ltd., Denmark (non-U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5464821		19951107
	WO 9216551		19921001
APPLICATION INFO.:	US 1993-122510		19930924 (8)
	WO 1992-DK95		19920325
			19930924 PCT 371 date
			19931216 PCT 102(e) date

	NUMBER	DATE
PRIORITY INFORMATION:	DK 1991-532	19910325
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	Granted	
PRIMARY EXAMINER:	Warden, Jill	
ASSISTANT EXAMINER:	Huff, Sheela J.	
LEGAL REPRESENTATIVE:	Banner & Allegretti, Ltd.	
NUMBER OF CLAIMS:	9	
EXEMPLARY CLAIM:	1	
NUMBER OF DRAWINGS:	4 Drawing Figure(s); 4 Drawing Page(s)	
LINE COUNT:	909	
CAS INDEXING IS AVAILABLE FOR THIS PATENT.		
SUMM	E is cysteine or a cysteine homologue, the sulphydryl group being free or substituted,	
DETD	. . . of Pharmaceutics 52, p. 255 (1989), Bundgaard, H. An example of	
	the use of additives is given in "Evaluation of mucoadhesive polymers in ocular drug delivery. 1. Viscous solutions", Pharmaceuticals Res. 8, p. 1039 (1991), Davies, N. M. et al.	

L5 ANSWER 45 OF 51 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1999:758076 CAPLUS
DOCUMENT NUMBER: 132:298491
TITLE: **Thiolated polymers: a new generation of mucoadhesive polymers**
AUTHOR(S): Bernkop-Schnuerch, A.
CORPORATE SOURCE: Cent. of Pharm., Inst. of Pharm. Technol., Univ. of Vienna, Vienna, A-1090, Austria
SOURCE: Farmacevtski Vestnik (Ljubljana) (1999), 50(Pos. Stev.), 268-269
PUBLISHER: Slovensko Farmacevtsko Drustvo
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
TI **Thiolated polymers: a new generation of mucoadhesive polymers**
AB A review with 4 refs. of the mucoadhesion, cohesiveness, and penetration-enhancing capabilities of **thiomers** (**thiolated polymers**) and their action in inhibiting Zn proteinases. These polymers include conjugates of cysteine with polycarbophil, chitosan, and Na CM-cellulose, and are believed to interact with cysteine-rich subdomains of mucus glycoproteins.
ST review **thiolated polymer bioadhesive**
IT Adhesives
(biol.; **thiolated polymers: new generation of mucoadhesive polymers**)
IT **Thiols** (organic), biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(conjugates with polymers; **thiolated polymers: new generation of mucoadhesive polymers**)
IT Mucus
(**thiolated polymers: new generation of mucoadhesive polymers**)
IT Polymers, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**thiolated; thiolated polymers: new generation of mucoadhesive polymers**)

PATFULL
 ACCESSION NUMBER: 1999:113787 USPATFULL
 TITLE: Use of fatty acid esters as bioadhesive substances
 INVENTOR(S): Hansen, Jens, Allerod, Denmark
 Nielsen, Lise Sylvest, Copenhagen .O slashed., Denmark
 Norling, Tomas, Lyngby, Denmark
 PATENT ASSIGNEE(S): GS Development AB, Malmo, Sweden (non-U.S.
 corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5955502		19990921
APPLICATION INFO.:	US 1997-829496		19970327 (8)
RELATED APPLN. INFO.:	Division of Ser. No. US 1997-462222, filed on 5 Jun 1997		

	NUMBER	DATE
PRIORITY INFORMATION:	DK 1994-37	19940330
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	Granted	
PRIMARY EXAMINER:	MacMillan, Keith D.	
LEGAL REPRESENTATIVE:	Watov & Kipnes, P.C.	
NUMBER OF CLAIMS:	22	
EXEMPLARY CLAIM:	1	
NUMBER OF DRAWINGS:	7 Drawing Figure(s); 6 Drawing Page(s)	
LINE COUNT:	2331	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

SUMM During the last decade increased attention has been given to the possibility of using bioadhesive/**mucoadhesive polymers** for drug delivery purposes. It is believed that several problems associated with conventional controlled release drug delivery systems may be.

DETD mucopolysaccharides such as, e.g., **thiomucosee**,
 DETD . . . Hounslow, U.K.) is a high molecular weight poly(acrylic acid) copolymer loosely cross-linked with divinyl glycol. On account of its known excellent **mucoadhesive** properties, this polymer serves as a reference. Before testing in the above-mentioned tensiometric test, a polycarbophil gel is prepared by mixing polycarbophil with. . .

L5 ANSWER 40 OF 51 USPATFULL
 ACCESSION NUMBER: 1999:78708 USPATFULL
 TITLE: Urethane-containing aminosteroid compounds
 INVENTOR(S): Yu, Chia-Nien, Norwich, NY, United States

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ACCESSION NUMBER: 2000:672530 CAPLUS
DOCUMENT NUMBER: 134:136581
TITLE: **Mucoadhesive thiolated polymers**: Synthesis and in vitro evaluation of chitosan-thioglycolic acid conjugates
AUTHOR(S): Kast, C. E.; Freudl, J.; Bernkop-Schnurch, A.
CORPORATE SOURCE: Center of Pharmacy, Institute of Pharmaceutical Technology and Biopharmaceutics, University of Vienna,
Vienna, A-1090, Austria
SOURCE: Proceedings of the International Symposium on Controlled Release of Bioactive Materials (2000), 27th, 1222-1223
PUBLISHER: Controlled Release Society, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT

TI **Mucoadhesive thiolated polymers**: Synthesis and in vitro evaluation of chitosan-thioglycolic acid conjugates
AB The covalent attachment of thioglycolic acid to cationic chitosan leads to polymers exhibiting strongly improved mucoadhesive properties. Due to the formation of inter- and/or intrachain disulfide bonds based on an oxidn. process, the cohesive properties of the polymer could by improved as well.
ST **thioglycolate** chitosan mucoadhesive drug
IT Drug delivery systems (oral, bioadhesive; prepn. and in vitro evaluation of chitosan-thioglycolic acid conjugates for mucoadhesive drug delivery systems)
IT 68-11-1DP, **Thioglycolic acid**, conjugates with chitosan 9012-76-4DP, Chitosan, conjugates with thioglycolic acid
RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. and in vitro evaluation of chitosan-thioglycolic acid conjugates for mucoadhesive drug delivery systems)

L5 ANSWER 32 OF 51 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:350505 CAPLUS
DOCUMENT NUMBER: 136:107353
TITLE: In vitro evaluation of matrix tablets based on
thiolated polycarbophil
AUTHOR(S): Clausen, Andreas E.; Bernkop-Schnurch, Andreas
CORPORATE SOURCE: Center of Pharmacy, Institute of Pharmaceutical
Technology and Biopharmaceutics, University of
Vienna,
Vienna, Austria
SOURCE: Pharmazeutische Industrie (2001), 63(3), 312-317
CODEN: PHINAN; ISSN: 0031-711X
PUBLISHER: Editio Cantor Verlag
DOCUMENT TYPE: Journal
LANGUAGE: English
REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR
THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT
TI In vitro evaluation of matrix tablets based on thiolated
polycarbophil
AB Based on thiolated polycarbophil, a mucoadhesive peptide drug
delivery system with improved stability and release properties has been
established. Mediated by a carbodiimide, L-cysteine was covalently
linked to polycarbophil (PCP). The amt. of cysteine moieties on the polymer was
in the range of 72.6.+-5.8 .mu.mol/g polymer. Disintegration studies
with tablets of thiolated PCP (PCP-Cys) demonstrated a stability
for 48.3.+-1.5 min at 37.degree. in 100 mM Tris-HCl pH 6.8, whereas
tablets of the corresponding unmodified polymer (PCP) disintegrated
within a time period of 13.8.+-1.6 min (mean .+- SD, n = 3). During these
disintegration studies the amt. of thiol groups decreased in
tablets consisting exclusively of PCP-Cys by 80.0.+-4.5%, suggesting
that the formation of inter- and/or intramol. disulfide bonds is responsible
for this strongly improved stability of tablets based on the
thiolated polymer. Further expts. demonstrated that this decrease
in thiol groups can be lowered to 64.2.+-0.8% by substituting
60 % of the thiolated polymer by mannitol. Release studies of
the fluorescence labeled model drug insulin showed that an almost
zero-order release kinetic can be provided by the use of thiolated
polycarbophil as carrier matrix. The results represent helpful
information in order to improve the stability and release properties of
matrix tablets based on mucoadhesive polymers.
ST insulin thiol polycarbophil tablet control release;
polycarbophil tablet mucoadhesive peptide delivery
IT Drug delivery systems
(tablets, controlled-release, mucoadhesive peptide-; thiolated
polycarbophil matrix tablets in vitro evaluation)
IT Dissolution
(thiolated polycarbophil matrix tablets in vitro evaluation)
IT 25952-53-8, 1-Ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride
RL: RCT (Reactant); RACT (Reactant or reagent)
(thiolated polycarbophil matrix tablets in vitro evaluation)
IT 7048-04-6DP, L-Cysteine hydrochloride monohydrate, conjugates with
polycarbophil 9003-97-8DP, Polycarbophil, conjugates with cysteine
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological
study); PREP (Preparation); USES (Uses)

(thiolated polycarbophil matrix tablets in vitro evaluation)
IT 69-65-8, Mannitol 9004-10-8, Insulin, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(thiolated polycarbophil matrix tablets in vitro evaluation)

L5 ANSWER 33 OF 51 USPATFULL
ACCESSION NUMBER: 2000:64898 USPATFULL
TITLE: Enzyme inhibitors
INVENTOR(S): McIver, John McMillan, Cincinnati, OH, United States
Underiner, Todd Laurence, Cincinnati, OH, United States
States Bates, Timothy, Cincinnati, OH, United States
PATENT ASSIGNEE(S): The Procter & Gamble Company, Cincinnati, OH, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6066673		20000523
APPLICATION INFO.:	US 1998-41196		19980312 (9)
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	Granted		
PRIMARY EXAMINER:	Padmanabhan, Sreeni		
LEGAL REPRESENTATIVE:	Echler, Sr., Richard S., McDow-Dunham, Kelly L., Hersko, Bart S.		
NUMBER OF CLAIMS:	22		
EXEMPLARY CLAIM:	1		
LINE COUNT:	2685		

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ACCESSION NUMBER: 2001:93131 USPATFULL
TITLE: Solid carriers for improved delivery of active ingredients in pharmaceutical compositions
INVENTOR(S): Patel, Mahesh V., Salt Lake City, UT, United States
PATENT ASSIGNEE(S): Chen, Feng-Jing, Salt Lake City, UT, United States
Lipocene, Inc., Salt Lake City, UT, United States
(U.S.
corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6248363	B1	20010619
APPLICATION INFO.:	US 1999-447690		19991123 (9)
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	GRANTED		
PRIMARY EXAMINER:	Spear, James M.		
LEGAL REPRESENTATIVE:	Reed, Dianne E. Reed & Associates		
NUMBER OF CLAIMS:	57		
EXEMPLARY CLAIM:	1		
NUMBER OF DRAWINGS:	4 Drawing Figure(s); 4 Drawing Page(s)		
LINE COUNT:	3302		
CAS INDEXING IS AVAILABLE FOR THIS PATENT.			
DETD	. . . vaccine; salmetrol xinafoate; sinalide; small pox vaccine; solatol; somatostatin; sparfloxacin; spectinomycin; stavudine; streptokinase; streptozocin; suxamethonium chloride; tacrine hydrochloride; terbutaline sulfate; thiopeta; ticarcillin; tiludronate; timolol; tissue type plasminogen activator; TNFR:Fc; TNK-tPA; trandolapril; trimetrexate gluconate; trospectinomycin; trovafloxacin; tubocurarine chloride; tumor necrosis factor; typhoid.		

DETD **Mucoadhesive polymers and polymer**
-inhibitor conjugates, such as polyacrylate derivatives, chitosan, cellulosics, chitosan-EDTA, chitosan-EDTA-antipain, polyacrylic acid-bacitracin, carboxymethyl cellulose-pepstatin, polyacrylic acid-Bwoman-Birk inhibitor.

DETD . . . methanesulfonic acid, oxalic acid, para-bromophenylsulfonic acid, propionic acid, p-toluenesulfonic acid, salicylic acid, stearic acid, succinic acid, tannic acid, tartaric acid, thioglycolic acid, toluenesulfonic acid and uric acid, and where the base is a pharmaceutically acceptable base, such as an amino acid, . . .
methanesulfonic acid, oxalic acid, para-bromophenylsulfonic acid, propionic acid, p-toluenesulfonic acid, salicylic acid, stearic acid, succinic acid, tannic acid, tartaric acid, thioglycolic acid, toluenesulfonic acid, and uric acid;

CLM What is claimed is:
. . . vaccine; salmetrol xinafoate; sinalide; small pox vaccine; solatol; somatostatin; sparfloxacin; spectinomycin; stavudine; streptokinase; streptozocin; suxamethonium chloride; tacrine hydrochloride; terbutaline sulfate; thiopeta; ticarcillin; tiludronate; timolol; tissue type plasminogen activator; TNFR:Fc; TNK-tPA; trandolapril; trimetrexate gluconate; trospectinomycin; trovafloxacin; tubocurarine chloride; tumor necrosis factor; typhoid. . .
. . . vaccine; salmetrol xinafoate; sinalide; small pox vaccine; solatol; somatostatin; sparfloxacin; spectinomycin; stavudine; streptokinase; streptozocin; suxamethonium chloride; tacrine hydrochloride; terbutaline

sulfate; thiopeta; ticarcillin; tiludronate; timolol; tissue
type plasminogen activator; TNFR:Fc; TNK-tPA; trandolapril;
trimetrexate
gluconate; trospectinomycin; trovafloxacin; tubocurarine chloride;
tumor
necrosis factor; typhoid. . .

L5 ANSWER 27 OF 51 USPATFULL

PATFULL
ACCESSION NUMBER: 2001:190748 USPATFULL
TITLE: Triglyceride-free compositions and methods for
enhanced absorption of hydrophilic therapeutic agents
INVENTOR(S): Patel, Mahesh V., Salt Lake City, UT, United States
PATENT ASSIGNEE(S): Chen, Feng-Jing, Salt Lake City, UT, United States
Lipocene Inc., Salt Lake City, UT, United States (U.S.
corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6309663	B1	20011030
APPLICATION INFO.:	US 1999-375636		19990817 (9)
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	GRANTED		
PRIMARY EXAMINER:	Page, Thurman K.		
ASSISTANT EXAMINER:	Channavajjala, Lakshmi		
LEGAL REPRESENTATIVE:	Reed, Dianne E.Reed & Associates		
NUMBER OF CLAIMS:	170		
EXEMPLARY CLAIM:	1		
LINE COUNT:	4371		
CAS INDEXING IS AVAILABLE FOR THIS PATENT.			
SUMM	vaccine; salmetrol xinafoate; sincalide; small pox vaccine; solatol; somatostatin; sparfloxacin; spectinomycin; stavudine; streptokinase; streptozocin; suxamethonium chloride; tacrine hydrochloride; terbutaline sulfate; thiopeta; ticarcillin; tiludronate; timolol; tissue type plasminogen activator; TNFR:Fc; TNK-tPA; trandolapril; trimetrexate gluconate; trospectinomycin; trovafloxacin; tubocurarine chloride; tumor necrosis factor; typhoid.		
SUMM	Mucoadhesive polymers and polymer -inhibitor conjugates, such as polyacrylate derivatives, chitosan, cellulosics, chitosan-EDTA, chitosan-EDTA-antipain, polyacrylic acid-bacitracin, carboxymethyl cellulose-pepstatin, polyacrylic acid-Bowman-Birk inhibitor.		
SUMM	. . . maleic acid, oxalic acid, para-bromophenylsulfonic acid, propionic acid, p-toluenesulfonic acid, salicylic acid, stearic acid, succinic acid, tannic acid, tartaric acid, thioglycolic acid , toluenesulfonic acid, uric acid, and the		

L5 ANSWER 18 OF 51 USPATFULL
ACCESSION NUMBER: 2002:224440 USPATFULL
TITLE: Polymer grafting by polysaccharide synthases
INVENTOR(S): DeAngelis, Paul L., Edmond, OK, United States
PATENT ASSIGNEE(S): The Board of Regents of the University of Oklahoma,
Norman, OK, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6444447	B1	20020903
APPLICATION INFO.:	US 1999-437277		19991110 (9)
RELATED APPLN. INFO.:	Continuation-in-part of Ser. No. US 1999-283402, filed on 1 Apr 1999		

	NUMBER	DATE
PRIORITY INFORMATION:	US 1998-107929P	19981111 (60)
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	GRANTED	
PRIMARY EXAMINER:	Nashed, Nashaat T.	
LEGAL REPRESENTATIVE:	Dunlap, Codding & Rogers, P.C.	
NUMBER OF CLAIMS:	48	
EXEMPLARY CLAIM:	1	
NUMBER OF DRAWINGS:	11 Drawing Figure(s); 11 Drawing Page(s)	
LINE COUNT:	2329	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

DETD . . . by matrix-assisted laser desorption ionization time-of-flight mass spectrometry. Sugars in water were mixed with an equal volume of 5 mg/ml 6-azo-2-thiothymine in 50% acetonitrile/0.1% trifluoroacctic acid, and rapidly air-dried on the target plate. The negative ions produced by pulsed nitrogen laser. . .
DETD . . . development both in academia and in industry. The first generation of bioadhesive drug delivery systems (BBDS) were based on so-called **mucoadhesive polymers**, i.e. natural or

L5 ANSWER 12 OF 51 USPATFULL
ACCESSION NUMBER: 2002133237 USPATFULL
TITLE: BIOADHESIVE HYDROGELS WITH FUNCTIONALIZED DEGRADABLE
CROSSLINKS
INVENTOR(S): MARCHANT, NANCY S., MEDINA, OH, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2002068087	A1	20020606
	US 6514535	B2	20030204
APPLICATION INFO.:	US 1999-316688	A1	19990521 (9)
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	APPLICATION		
LEGAL REPRESENTATIVE:	NESTOR W. SHUST, HUDA&SHUNK CO., L.P.A., 7 WEST BOWERY STREET, SUITE 808, AKRON, OH, 44308-1138		
NUMBER OF CLAIMS:	36		
EXEMPLARY CLAIM:	1		
LINE COUNT:	1161		
CAS INDEXING IS AVAILABLE FOR THIS PATENT.			
SUMM	[0009] Yip discloses in U.S. Pat. No. 4,898,824 a crosslinked polyacrylamide- sulphydryl polymer for immobilization of biologically active substances. Saffran, et al. disclose in U.S. Pat. No. 4,663,308 high molecular weight polymers.		
SUMM	. . . body are coated with a mucus membrane. The ability of a material to 'stick' to a mucous membrane is termed mucoadhesion or bioadhesion. Polymers capable of hydrogen bonding are known to be the best at bioadhesion. Crosslinked polyacrylic acid hydrogels such as Carbopol.RTM. (B. . .		
SUMM	. . . bioadhesive composition, wherein the crosslink is at least one member selected from the group consisting of disulfides, esters, peptides, and thiols .		
SUMM	. . . in forming reversible crosslinked electrophoresis gels. Alternatively the amino acid cysteine and the disulfide version cystine may be acryloated other thiol /disulfide combinations can be used as long as there is a polymerizable functionality attached (e.g., acryl or allyl). Controlled molecular weight.		
SUMM	. . . crosslink two portions of the polymer network. This form of sulfur is relatively stable but can be reduced to the sulphydryl group thus breaking the crosslink. It may also be oxidized to break the crosslink by forming sulfonic acid or sulfate. . . may be oxidized		
to	form disulfide crosslinks. Polymers may be made using either a disulfide based monomer system or a thiol based monomer system. For example, in a low molecular weight hydrophilic polymer with thiol groups, the thiol group is oxidized to give a crosslinked gel. It may be envisioned that drug may be distributed through a low.		
SUMM	. . . or oxidation of the crosslinks. One major power of the disulfide system is that it undergoes exchange reactions. A free thiol may exchange into a disulfide bond and cause rearrangement. This may be used in bioadhesive applications where binding to mucin disulfide bonds or externally available thiols and disulfides of proteins may be exchanged.		
SUMM	[0072] Any thiol containing reagents such as dithiothreitol, dithioerythritol, 2 mercaptoethanol and mercaptoethylamine, and cysteine can serve as reducing agents for disulfides. Complete conversion of disulfide to thiol can be achieved with excess reducing		

agents. With Dithiothreitol, low level is enough to drive the reaction to completion because. . . a carbomer like matrix. The apparent pH

of the mixture will also influence the ability to exchange the disulfide to

sulphydryl. The colon is known to be a reducing environment and there may be a different rate of reduction/oxidation depending upon. . .

SUMM [0073] In order to re-establish a disulfide crosslink, the **sulphydryl** bond is oxidized to the disulfide. Any oxidizing agent such as air, iodide or hydrogen peroxide, is capable of oxidizing.

SUMM [0074] One could also envision making a system with a **sulphydryl** as a method to bind an active drug by forming a disulfide that is released upon reduction, or forming a. . .

SUMM [0079] 3. Disulfide: Cleaved by reducing agents and enzymatic r